Comparison of spray drying and hot melt extrusion as methods to prepare amorphous solid dispersions

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Abstract:

Most of the orally administered drugs in the development today are having low solubility, which then leads to high doses and higher frequency of dosing. Amorphous solid dispersions (ASDs) are approaches in the pharmaceutical industry, where the substance is molecularly dispersed in excipient, generally polymer, matrix. The advantage of amorphous, as compared to crystalline form, is that lower energy is required for dispersion of the molecules into the solvent, therefore achieving higher apparent solubility and providing faster dissolution. Several methods are available to prepare ASDs, namely precipitation, spray drying or hot melt extrusion. Spray drying and hot melt extrusion also have the possibility to produce continually, decreasing the batch variability, lowering dead times needed for cleaning, while also being possible to scale them up. Possible problems include recrystallization and the thermal damage of the drug due in SD and HME. The choice of polymer is also broad, including hypromelloses (HPMCAS, HPMCP, HPMC), methyl acrylates (Eudragit) or polyvinylpyrrolidone (Kollidons). The choice of polymer, as well as the ratio of drug to polymer, is selected by screening and the choice between having high drug amount (leads to crystallization) and high polymer amount (increases the dose size). In this work, we will compare the dissolution profile, amorphization and the influence of tablet preparation of a drug product with several polymers produced by SD and HME, as well as using computational fluid dynamics simulation to show the velocity and temperature profiles in SD and stresses in HME.